THE EVIDENCE FOR TUBERCULOSIS IN THE EASTERN MEDITERRANEAN: PAST AND CURRENT RESEARCH, AND FUTURE PROSPECTS

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Abstract

Tuberculosis (TB) is an infectious disease that had a significant impact on past human populations and continues to plague humans in both developing and developed countries. Recent research has noted that the first evidence for TB comes from Italy and is dated to 5800±90BC but that skeletal data from Egypt, Israel and Jordan in the eastern Mediterranean also have early dates. This paper documents the extant data for TB from these countries, considers the socio-cultural implications for the populations concerned, and makes recommendations for the study of TB in the future. We discuss the relevance of evidence for TB in animal remains from early domesticates in the Eastern Mediterranean and question the hypothesis that TB was transmitted from animals to humans at the time of domestication. The use of ancient DNA analysis to diagnose TB in skeletal and mummified samples is noted.

Key words: Ancient TB, Jordan, Israel, Egypt

Introduction

Tuberculosis (TB) is an infectious disease of immense importance to society today as it was in our ancestor's world. It is the most frequently encountered myco-bacterial disease (Collins et al., 1997:4), and is high in the global list of major causes of death (Grange, 1999). Among the infectious diseases, TB is the single most important cause of death, and the World Health Organisation estimates a world total of 8.08 million new cases per year. Since the mid-1980s there has been a gradual increase in TB cases globally, a picture that has been complicated by drug resistance (American Lung Association Conference 1996). Estimates for 2002 suggest there were 29 deaths from TB per 100,000 population, 141 per 100,000 cases (all forms), and 63 per 100,000 cases (smear positive) (World Health Organisation, 2004). Social concern has not however kept pace, as Farmer (1999:213), in a book on contemporary plagues, reports that 'Interest in TB is at an all-time low which is certainly striking if deaths are at an all time high.'

Re-emergence of TB is related to sociological, ecological and geographic changes and problems, as much as to molecular and microbiological phenomena (Mayer, 2000). Mayer also identifies five primary reasons why diseases such as TB may be re-emerging: 1) cross-species transfer, 2) spatial diffusion, 3) pathogenic evolution or change in the structure and immunogenicity of earlier pathogens, 4) new descriptions of pathogens that have been present for years but have been "newly" recognised, and 5) a change in human-environment relationships (*ibid*:940). In addition, he notes trade and transportation, contamination of water and food, migration and mobility and climate change as major factors in (re)emerging infectious diseases. In the Eastern Mediterranean incidence rates (all cases) most recently reported are 29/100,000 population for Egypt, 5/100,000 population for Jordan, and 10 /100,000 population for Israel (World Health Organisation Global TB Database 2004). Compared to other countries these rates are low, with global rankings being 52nd for Egypt, 143rd for Israel and 160th for Jordan. Of course, it is not known how common TB was in the past in these countries because our data are incomplete.

The frightening description of TB in many countries today cannot begin to tell us how devastating this disease must have been for our distant ancestors when effective treatment was unavailable. Past people can speak to us through their remains but this belies the chest pain, shortness of breath, weakness, and loss of appetite and fever they may have experienced during the course of their disease, and how it may have compromised their normal day to day activities. We can only speculate about the impact of TB on these populations by considering how the disease was described and depicted in writing and paintings, as the primary hard evidence for TB rests in skeletal and mummified remains from archaeological sites. The Eastern Mediterranean is an area of the world with a rich archaeological and historical heritage so tracing the origin, evolution and the history of TB has great potential.

By considering the context in which people with TB lived in certain times and places during humankind's history, we may begin to address questions crucial for understanding the co-evolution of humans and myco-bacterial disease. What factors in the Eastern Mediterranean predisposed people in the past to contracting TB? Was it poor levels of hygiene, living conditions in their houses, what they ate, the animals they kept, or their occupations? This paper takes a

"broadbrush" view of TB in the Eastern Mediterranean (Egypt, Israel and Jordan), highlighting present status and future potential. First, an overview will be given of facts about TB that are of relevance.

TB: Facts

(i) The causative organisms

TB is an infectious disease caused by the genus *Mycobacterium* that affects human and non-human mammals. *M. tuberculosis, M. bovis*, along with *M. africanum* and *M. microti*, make up the 'TB complex' and are closely related organisms. Vincent and Gutierrez Perez (1999) further define *M. tuberculosis* as an agent of TB in humans and a small number of animals, *M. bovis* as the agent of TB in animals and in some humans, *M. africanum* the agent of TB in humans in some African countries, and *M. microti* the agent of TB in voles (probably a very rare and extinct vole bacillus). *M. africanum* is not a true species but a heterogeneous group of strains of *Mycobacteria* with properties intermediate between *M. tuberculosis* and *M. bovis* which were first isolated in equatorial Africa (Grange and Yates, 1994). Of course this organism may have particular relevance for TB in the Eastern Mediterranean, but different *Mycobacteria* could lead to similar skeletal changes, and the only way of differentiating the organisms would be to use ancient DNA analysis. Recent research has started to explore this with some promising results (Mays et al., 2001). Interestingly too, Zink et al. (2003, 2005) have through ancient DNA analysis found that, in samples from Egyptian mummies dated to since c. 2050 BC and c. 500 BC, *M. africanum* and *M. tuberculosis* were the most common organisms causing TB. They suggest that *M. tuberculosis* may have originated from a precursor complex probably related to *M. africanum*, thus confirming an earlier phylogenetic argument based upon molecular characterizations of contemporary members of the *M. tuberculosis* complex (Brosch et al., 2002).

(ii) Transmission and pathogenesis

TB is most commonly transmitted by infected droplets from the lungs of an infected person to a non-infected person (Figure 1). This occurs through coughing, sneezing, and even speaking and singing (Vincent and Gutierrez Perez, 1999:140). Eating or drinking infected animal products can also introduce the disease via the gastrointestinal system. TB depends on infected human populations living in close proximity to each other in settled communities or upon contact with infected wild or domesticated animals. Again, this has relevance for identifying the underlying cause for the first appearance of TB in the Eastern Mediterranean. Was it dependent on wild or domesticated animals and/or overcrowded settled communities?

Primary TB may be established, with the possibility of later activation following re-exposure to the disease (secondary or post-primary TB). Changes in a person's resistance or immune system or re-infection can cause reactivation of a latent infection. Once post-primary TB is established, skeletal changes may occur and could be identified. We assume that, in the initial stages of its establishment in the world's populations, TB was probably more virulent than in later years as resistance to the bacteria developed. This has implications for its appearance in human remains from archaeological sites. People would have died rapidly from the infection in the early years of its development, without bone changes. Biomolecularly, however, it may be possible to detect those people in a population, and thus push back the earliest dates for TB both in the Eastern Mediterranean and the rest of the world.

(iii) Risk factors

The list of TB risk factors is very long. Today, population growth and increased density, immunosuppression, age, HIV, malnutrition, pregnancy, trauma and malignancy and many "environmental" factors, such as war, migration and mass disasters can all make people more vulnerable to TB. However, the HIV, Aids, multidrug resistance, poverty and lack of access to treatment are underlying factors today. The following factors are considered more relevant for past populations.

a) Sex, age and ethnicity

Data suggest that more males than females are infected with TB today (Kumaresan et al., 1996 in Murray and Lopez, 1996). Most work also suggests that males get sick more often than females (Hudelson, 1996:393; Borgdorff et al., 2000). Male and female lifestyles may also be influential, but sex hormones are also relevant (Pollard and Hyatt, 1999:6). Males are more sensitive to the environment, have a higher death rate in the first few weeks of life, and are more ill in childhood. Females are more buffered against the environment during growth (Stinson, 1985:127), their immune response is better in adulthood, and prognosis for recovery from illness is enhanced (Stini, 1985). In the past, if a female had effective resistance to TB she may not have ever developed bone changes, but a good immune response may have allowed her to live long enough to develop chronic bone damage (Wood et al., 1992).

In contemporary groups, birth to five years, 15-30 years, and 60 years+ are the age groups most frequently affected (Johnston, 1995:29) - resistance is lowest at these times. As children usually contract TB from adults via inhalation and consuming infected animal or breast milk, TB in children may be a good indicator of frequency in adults. If people did not live long in the past then only TB in infancy, puberty and early adulthood may be expected. Correlating exact age at death with TB occurrence in the past is not easy; ageing adult skeletons remains a problem, and identifying age of onset for bony involvement is simply impossible. In Jordan, Israel and Egypt today more males than females are affected, with

Figure 1: Sneezing can enable bacteria of tuberculosis to be transmitted via droplet infection (by permission of Pia Bennike).

the highest rates seen in the 40-60 year age group in both sexes (Egypt), 40-50 years for males and around 50 years for females in Israel, and around 60 years of age for both sexes in Jordan (World Health Organisation 2004). There is no agreement about the relationship of genetic makeup and TB, but Newport and Levin (1999:120) suggest, '...it seems likely that the development of mycobacterial infection in man will prove to be as much dependent on the genetic make-up of the host, as the virulence of the bacteria' (but socioeconomic factors will much influence its occurrence too). For example, it is suggested that Jewish groups are most resistant (Btesh, 1958; Rakower, 1953) and blacks are most susceptible (Roth, 1938; Stead, 1992) to clinical disease and death from human TB. In another study by Davies *et al.* (1984), in England and Wales the annual rates for skeletal TB were 29/100,000 for people originating from the Indian subcontinent (ISC) and only 0.34/100,000 for white populations. Of course, researchers can estimate a person's origin archaeologically through stable isotope analysis (Katzenberg, 2000; Price et al., 2001; Budd et al., 2004; Montgomery et al., 2005), ancient DNA (Stone, 2000), and morphological features of the skeleton (Krogman and Iscan, 1986) and teeth (Scott and Turner, 1997), although no research yet has considered differential susceptibility of archaeologically known groups to TB.

b) Diet, poverty and social status

A balanced diet, preferably with adequate levels of protein, is recommended for a strong immune system to resist TB (Dubos and Pierce, 1948; McMurray and Barlow, 1992). Poor nutrition influences the incidence, severity, duration and outcome of TB (Charlton and Murphy, 1997). Recent work has also suggested that Vitamin D lack may also be related to the occurrence of TB in humans, as it is responsible for suppressing intracellular growth of *M. tuberculosis* (Wilkinson et al., 2000). In some countries levels of sunlight and vitamin D in the diet are adequate, and the immune system can contain the infection (Davies, 1995:116). A combination of a vegetarian diet and lack of sunlight may, however, lead to low D levels in people who migrate. A study of children with TB in Egypt suggested that vitamin D therapy, along with antituberculous drugs, was effective (Moros et al., 1998).

TB is a "disease of poverty", and a good indicator of general health (Nichter, 1997). A healthy living environment, no crowding, and a nutritious diet are key to prevention. Today, the poor are usually found in urban areas, are old, unemployed and homeless, and may be drug and alcohol abusers (Moore Gillon, 1998:385). In the past, certainly in more recent periods, poor people existed in rural and urban environments. However, TB can also cut across social barriers (Rothman, 1994:2), and social status will affect TB risk and prognosis. Occupation, education and income are the three most common indicators used for predicting health status today (MacIntyre, 1998:20). Poverty also compromises access to health care facilities. The basic human need of shelter, its state of repair, insulation, ventilation, heating, size and number of rooms, cooking facilities and sanitation are

also relevant (Hunt, 1997:157). Lack of space, ventilation, sunlight, and poor sanitation can lead to TB. Population density is highly relevant to the contraction of TB via droplet infection. A study of the relationship between density and frequency of TB is possible today, but for the past it is more difficult when exact population density is unknown. McGrath (1988) estimates a social network of 180-440 people is needed to achieve a stable host-pathogen relationship necessary for TB to become endemic. The earliest convincing Old World cases of bone TB occur in sedentary Neolithic groups where increased population density would have been the case (Roberts and Buikstra, 2003).

(c) Travel and migration

Travel provides the potential for TB to be transmitted to previously unexposed populations. Migration and immigration are a part of human history. People have always moved to access better resources and work, and to move away from conflict areas; they can also carry diseases to places that have never encountered them before. Travel provides the potential for TB to be transmitted to previously unexposed populations. People who have moved, or who are in transit, also experience a changed relationship with their environment, and different health problems are encountered. As recently as 1950, TB was introduced to Inuit Eskimos of Northern Canada (Grzybowski et al., 1976 in Davies, 1995), and Davies (*ibid*) regards immigration as one of the single most important causes of increases in TB in most developed countries today. For example, in Israel today, immigration of people from countries highly endemic for TB (e.g. former Soviet Union) are raising TB rates and drug resistant strains, although there is little evidence for spread of TB to the host population (Chemtob et al., 2003). Bioarchaeological research is only just starting to look at mobility in a scientific way, but this has potential for future research on the origin and evolution of any of the infectious diseases.

(d) Occupation, including exposure to animals

Certain occupations carry increased risk for TB (Bowden and McDiarmid, 1994): unskilled labourers (e.g. food handlers), occupations increasing susceptibility through particulate pollution, irritation and inflammation of the lungs (e.g. mining and potting - Lancaster, 1990), and occupations increasing direct exposure likelihood (e.g. hospitals, prisons). Occupations in the past would have potentially predisposed people to TB, particularly those who worked in poorly ventilated, dusty and damp overcrowded conditions, and those who dealt with animal products such as food, horn, bone, and skins.

Exploiting animals (Figure 2) was probably very important to the development and maintenance of TB in the Eastern Mediterranean. Traditional interpretations of tuberculosis argue that the human form developed from mycobacterial zoonoses at the time of animal domestication (Cockburn 1963), a model that has recently been challenged by molecular evidence (Brosch et al., 2002; Zink et al., 2003, 2004, 2005). TB in domestic herd animals is usually caused by *Mycobacterium bovis*, a zoonosis (naturally transmissible disease between vertebrates and humans) spread through droplet infection (O'Reilly and Daborn, 1995). Wild (rarer) and domestic animals can be affected (Figure 3), but cattle are the most

Figure 2: Working with cattle while ploughing land.

Figure 3: Camels may also be affected by tuberculosis, a possible route of transmission for humans in the Eastern Mediterranean.

infectious to humans (Grange, 1995). Today an estimated 5% (50 million) of domesticated cattle are infected with bovine TB, with two thirds of domesticated cattle located in developing countries where there is little or no disease control (Thoen and Steele, 1995). *M. bovis* can also be excreted in the urine and faeces of humans and animals (Cosivi et al., 1995), and it can survive outside the host (O'Reilly and Daborn, 1995). Cultural practices that influence whether bovine TB infects humans include the use of cattle urine to wash utensils and mixing it with soil to create floors and wall surfaces. Cow dung is used for fuel, for fertilizer, and in building works (O'Reilly and Daborn, 1995). Age, sex, ethnicity, poverty, occupation, and exposure to infected animals could therefore be relevant to TB's first appearance and spread within the Eastern Mediterranean.

TB in the Old World

(i) Skeletal changes of TB

Detecting TB in skeletal remains primary evidence for the disease in the past but preservation may compromise diagnosis, and a skeletal sample can only display a part of the population's real health burden. TB may only affect the soft tissues, it may not cause bone changes before the person died, or it may not be able to make an impact on the skeleton because the person's immune system was very strong.

Skeletal changes are the result of post-primary TB spreading from its primary focus, but a population with no previous exposure will succumb quickly to death with no bone changes; many generations of exposure may lead to a stronger immune response, survival and visibility in the skeleton. Both *M. tuberculosis* and *M. bovis* may produce skeletal changes (the latter ten times more likely, Stead, 2000), but only c. 3-5% of people are usually affected (Resnick, 1995). The primary focus is the spine (Figures 4 and 5), and the hip and knee joints. Other (non-specific) changes may include new bone formation on the endocranial surface of the skull (Figure 6 - TB meningitis?), and bone formation on ribs (Figure 7 - pulmonary tuberculosis?). Studies of documented skeletal samples have suggested TB as the most likely cause for such non-specific changes on ribs (e.g. Roberts et al., 1994; Santos, 2000), and biomolecular work has found positive results for TB from skeletons with rib lesions (Haas et al., 2000), but this does not prove a direct association. Calcification of the lung pleura as a result of TB and other conditions has been found in some skeletons (e.g. see Donoghue et al., 1998; Roberts, 1999), but again it is impossible to specify TB as the cause of all pleural calcifications.

(ii) When did TB first occur?

TB required certain factors for it to occur in the past. About 10,000 years ago people began to settle in larger groups, produce their own food and domesticate animals and plants (Renfrew and Bahn, 1991). In the Near East farming was present by 8,000 years BC with sheep and goats domesticated (Smith, 1995). In fact, sheep and goats were probably more commonly domesticated than cattle because the local terrain was not accommodating to cattle (Hershkovitz and Gopher, 1999:447). Population densities remained relatively low during the Neolithic and we may therefore speculate that while present during the Neolithic, TB was probably more common during the Chalcolithic and more recent periods (*ibid*). Although the earliest convincing skeletal evidence of TB appears at the time animals were domesticated, TB can also be contracted from wild and feral animals. It could have, therefore, occurred in earlier animal and human populations. Closer contact of animals with each other, and with humans, as domestication proceeded could have helped the disease to establish itself (Cockburn, 1963). Whether this was *M. tuberculosis* or *M. bovis* is debated, but Brosch et al. (2002), looking at the genomic structure of tubercle bacilli, indicates that *M. tuberculosis* did not evolve from *M. bovis*, a conclusion confirmed by Zink and co-workers (2003, 2004, 2005), based upon studies of ancient pathogen DNA.

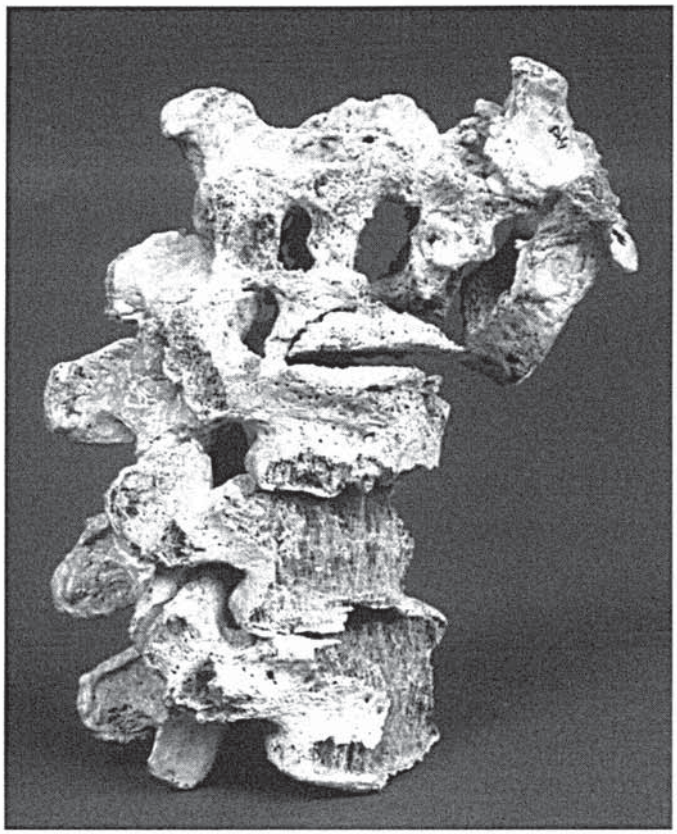

Figure 4: Pott's disease of the spine caused by tuberculosis.

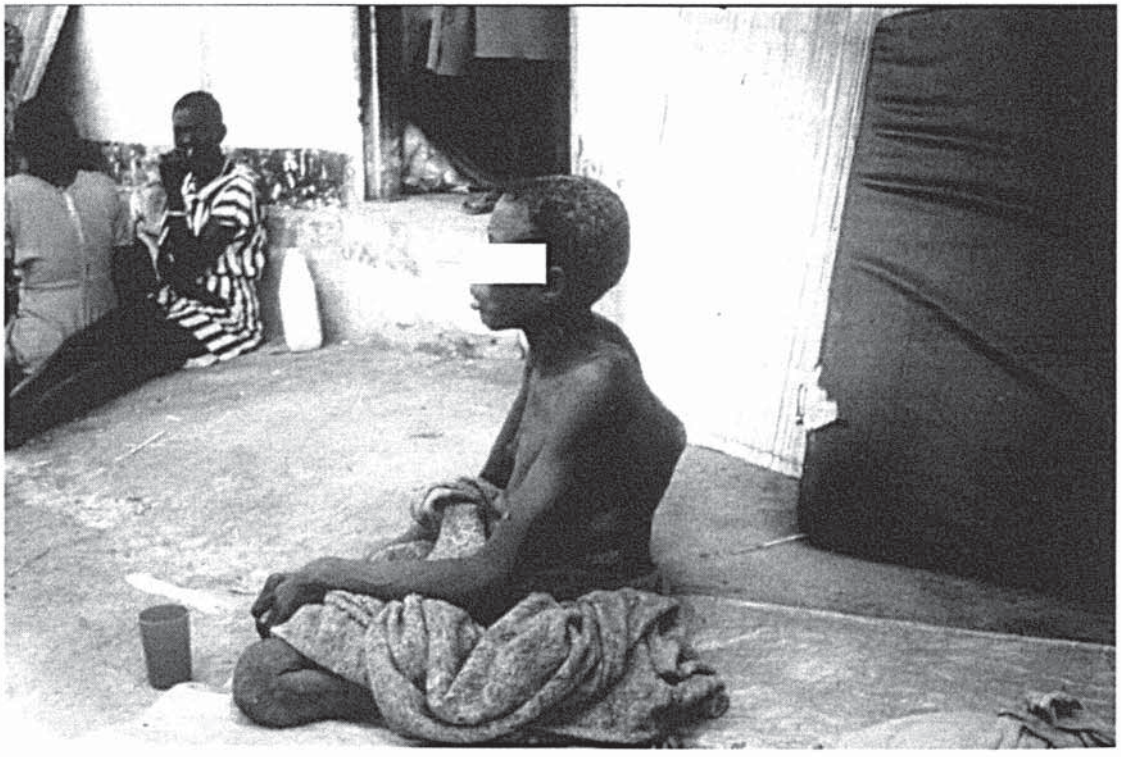

Figure 5: African woman with Pott's disease (by permission of Peter Davies).

Figure 6: New bone formation on the endocranial surface of the skull.

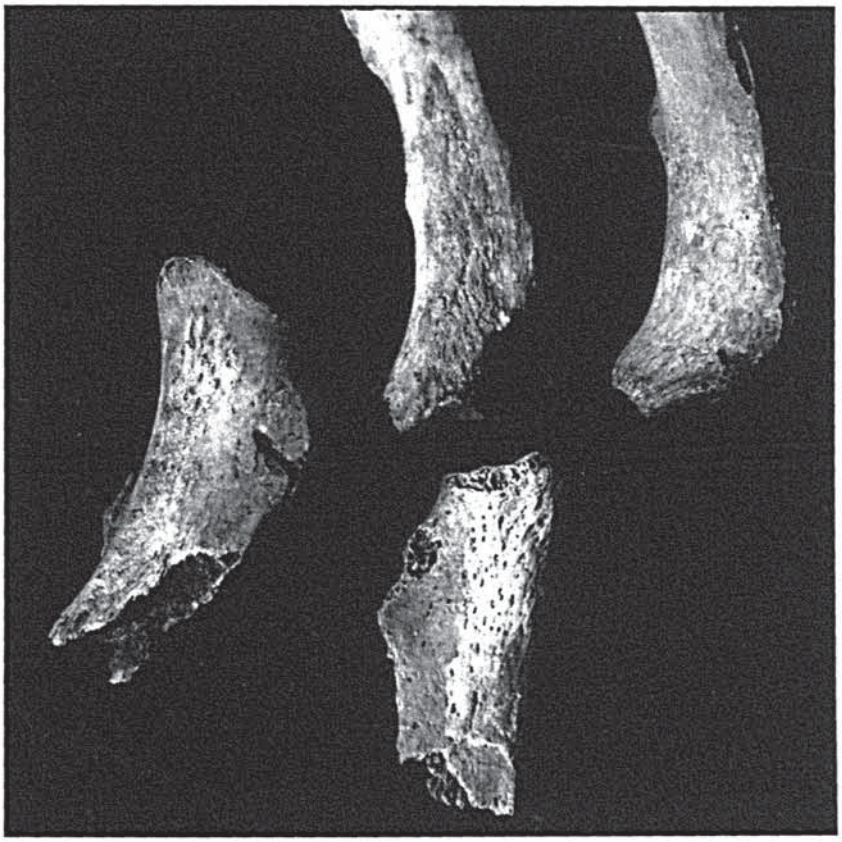

Figure 7: New bone formation on the visceral surfaces of the ribs.

What is the evidence for TB in non-human remains? Unfortunately there is very little convincing evidence for TB in non-human bones, something that badly needs addressing by the zooarchaeological community (but see Bathurst and Barta, 2004). It is surprising there is little TB reported. There is a considerable literature devoted to veterinary matters in Graeco-Roman sources, e.g. Columnella (1st century AD) and Hippocrates (5th century BC) – (Baker and Brothwell, 1980, Swabe, 1999). People have through time been aware of diseased animals and may have avoided, or discarded/killed them (Swabe, *ibid*:20). Was TB a problem in animals? When and where did it appear first (and decline)? Is it linked to the evidence for human TB at the same time in the same place, and how frequent was it? The study of pathological changes in animal remains is still very much in its infancy, but for studying the antiquity of TB it has a lot to offer. Nevertheless, a recent survey of archaeozoologists working on non-human skeletal remains in the eastern Mediterranean indicates there is either no interest in recording pathological changes in animal bones and/or they have never been noticed (Melinda Zeder, Andrew Garrard, Kevin Macdonald and Simon Davis, pers. comm., February 2005). There could, however, be potential for using biomolecuar methods of detecting TB in animals from the past.

When people started to settle in larger communities, human TB had the opportunity to become epidemic without extinguishing its hosts. Along with trade and migration, the ingestion of infected meat and milk from domesticated animals and, in general, closer contact with infected animals augmented risks of acquiring tuberculosis. However, increased use of fire for cooking (and, in effect, disinfecting) meat may have prevented transmission (Cohen, 1989:43). Dairy products have been a dietary staple for some, and there is a suggestion that lactose (milk sugar) intolerance (LI) may have made certain individuals less likely to contract TB. Domestication of animals may therefore be less important for spreading TB than the consumption of milk products (Hershkovitz and Gopher, 1999:447). Relevant too is that domestication of cattle in the Near East pre-dates TB in humans by 1000 years or so. Hunter-gatherers and Jewish populations today show high LI rates, which may explain the lack of TB in the Eastern Mediterranean. Flatz (1989) indicates that in studies of some groups, lactose intolerance rates are 73% for Egypt, 66% for Israelis and 80% for Arabs, and 79% for Jordanian agriculturists and 24% for Jordanian Bedouins. In North America and Northern Europe rates are much lower, but it is clear from a global view that lactose intolerance is the norm rather than being an abnormal state (Kretchner, 1993). This may explain the preponderance of TB in Northern Europe and America compared to the Eastern Mediterranean.

(iii) Studying the palaeopathology of TB

Important to note is that an absence of reported cases for regions and times may reflect a number of factors unrelated to ancient health. In addition, the distribution of archaeological excavations and physical anthropological studies varies enormously across the globe. Other limiting factors include the fact that criteria used by researchers to identify, and thus report skeletal TB, are not standard. Recognising TB in the past has begun to rely more on the successful extraction of ancient biomolecules specific to the TB causing organisms (e.g. Salo et al., 1994). When these techniques become more routine, are not fraught with questions of biomolecular survival and/or contamination, more realistic estimates of the absolute frequency of TB in past populations may be ascertained. Our previous work (Roberts and Buikstra, 2003) on skeletal TB in the Old World focused upon two areas: Northern Europe and the Mediterranean. For the purposes of this paper, the Mediterranean has been subdivided to reveal the Eastern Mediterranean countries of Egypt, Israel and Jordan.

a) Africa (Egypt and Nubia)

In sub-Saharan Africa there has been no evidence identified from human remains for TB (Santos, pers. comm. 2002). However, in Egypt and the Sudan, there exists reliable data on TB, beginning in the early 20th century (Elliott Smith and Ruffer, 1910). A male adult mummy named Nesperehăn from Thebes with a psoas abscess and spinal curvature (c1069-945 BC) firmly established the presence of TB in Egypt. Morse et al. (1964) also provided a survey of TB in Egypt in art evidence and human remains. Much discussion has ensued about whether deformed backs were an artistic style or really depicted a tuberculous spine (e.g. Filer, 1995:29). One example is a pre-Dynastic (c.4500-3000 BC) clay statuette of a man inside a clay bowl; he is thin and has a kyphotic spinal deformity (Schrumpf-Pierron, 1933). Other figurines, and bas-reliefs and carvings of pre-Dynastic and later periods show similar hunched backs (Morse et al., 1964; Morse, 1967). Morse et al., 1964:528), argue that the angular kyphosis depicted in Egyptian contexts is more convincing for TB than many of the rounded kyphotic deformities seen elsewhere in the world. Interestingly, Crubézy and Janin (1993) reported two pre-Dynastic skeletons from Adaima with Pott's disease of the spine, buried with pottery artefacts that had been fashioned to look like the spinal deformity.

Evidence of TB from Egyptian human remains was summarized by Derry (1938), who reported cases dating from 3300 to 1500 BC, all involving the spine. Morse et al. (1964) also discussed four examples from Nubia dating from the Middle Kingdom (c.2025-1700 BC), and 13 examples from Nagada in Upper Egypt of pre-Dynastic date (4500-3000 BC). Thus, TB could have been present in Egypt as early as 4500 BC. At the time of writing Morse et al. (1964:539) felt that it was likely, 'that the cases of possible TB ... represent only a part of those that have actually been found at Egyptian sites'. In summary, they discussed 31 cases of changes in skeletal

or mummified tissues resembling TB, including 13 from the Upper Egyptian site of Nagada (pre-Dynastic and later), 13 from Nubia (including six isolated vertebrae), one from Saqqara (3300 BC), and one from Deir-el-Bahri (1500 BC), ranging in age from 3700 to 1000 BC. However, Buikstra et al. (1993) suggest that the evidence was rather slender for pre-Dynastic TB in Egypt. They also reviewed many of Morse et al.'s (1964) cases with some confirmations, while in other cases differential diagnoses were considered. Strouhal (1987, 1989, 1991) described a 22-24 year old male with spinal TB from an early Christian site at Sayala, Nubia (4th century AD), and a middle aged male from a Middle Kingdom tomb at Abusir (2025-1700 BC). Walker (1991) has reported more recent cases of TB from Saqqara, one of the largest and most important cemeteries in Egypt (Buikstra et al., 1993). These Archaic to early Christian cases include a 19–20 year old female with spinal lesions (negative for *M. tuberculosis* DNA - Strouhal, 1999:455), and possible cranial TB in a child 4-5 years of age (negative for tuberculous ancient DNA - Strouhal, *ibid*:457). Strouhal (1999) also describes and discusses some previously reported cases, clearly indicating that controversy still remains for some diagnoses. Buikstra et al. (1993:46) also note that, 'While the presence of TB-like pathology remains convincing (in Egypt), its origin and impact on community health persist as unresolved issues'. Cattle had been domesticated by 6500 bp (MacDonald, 2000), long before the Dynastic period, thus providing a possible reservoir of tuberculous infection. Clearly, Egypt has a wealth of resources available for the reconstruction of the history of TB but much more work is needed.

During the 1970s researchers started to use methods of diagnosis of TB other than gross observations, including the direct isolation of tubercle bacilli in bone from a five year old child's mummy from the Upper Egyptian site of Dra Abu el-Naga dated to 1314-1085 BC (Zimmerman, 1979). In 1998, Crubézy et al. also managed to extract and amplify ancient DNA from the *M tuberculosis* complex from a 3400 BC pre-Dynastic Egyptian 12-14 year-old skeleton with Pott's disease from Adaima, Upper Egypt. More recently, Nerlich et al. (1997) and Zink et al. (1999) obtained a positive diagnosis of TB from the DNA isolated and sequenced from an infected lung of a mummy dated to between 1550 and 1080 BC (New Kingdom). This 35-year-old male individual was excavated from one of the tombs of the nobles at the necropolis of Sheik-Abd-el-Gurna/Thebes-West. In more recent research Zink et al. (2003, 2004) analysed bone and soft tissue samples from mummies from Thebes West Upper, Egypt. They found *M. africanum* in mummies dated to 2050-1650 BC, with *M. tuberculosis* in more recent burials (c.500 BC). They suggest that, certainly in Egypt, *M. tuberculosis* probably developed from *M. africanum* rather then *M. bovis*, thus supporting research by Brosch et al. (2002).

b) Israel

Few cases of TB have been reported in Israel, although it has been suggested (Zias, 1998) that, the prevalence of skeletal TB was and is low in Jewish communities who may have a genetic resistance to *Mycobacteria* when compared to populations living in identical conditions (Zias 1998:278). It is also suggested that cattle dairying did not play a very important part in Jewish history (Zias, 1998:283), that Jewish groups had lactose intolerance, and populations practised the ritual of examination of internal organs of animals to eliminate diseased ones. However, even if ritually excluded animals had been suffering from TB, milk could have been consumed before exclusion (Zias, 1998:289). A more plausible reason for a lower rate of tuberculous infection in Jewish groups may be their high frequency of Tay Sachs disease (Zias, 1998:291). This rare and fatal genetic disease confers resistance to TB. Clearly more work needs to be done on this hypothetical approach to TB frequency rates in Israel, although the possibility of achieving a long-term perspective is limited due to a strict moratorium on the excavation of skeletal material (Faulkner, 1998).

Nevertheless, Zias (1991a,b) reports on a possible case of TB (calcified pleura) in a 35-45-year-old male from the Monastery of John the Baptist (c.600 AD), near the Jordan River in the Judean Desert. A direct link between the pleura and TB however, cannot be proven. Zias (1998) also lists six more cases of TB from a variety of sites: Wado Makuq, Jericho (5450 BC; lumbar vertebrae), Vered Jericho (800 BC; lumbar vertebrae), Tel Marisha, Israel (200 BC; femur), East Talpiot, Israel (100 AD; femur), Qasr el-'Yehud, Jericho (900 AD; pleura), and various examples from Israel (Turkish, 16th-19th centuries). Unfortunately, none of these examples are illustrated or fully described but they are all from non-Jewish groups. Mitchell (1994 in Mitchell, 1999) also reports possible TB induced meningitis in an infant from the 12th-13th century AD site of Le Petit Gérin in the Kingdom of Jerusalem. New bone formation on the inside of the occipital bone may be the result of tuberculous induced meningitis, which Mitchell suggests is slow and insidious in its progress (1999:46). The question of whether a person could survive TB induced meningitis long enough for bone formation to occur is, however, a subject of debate (Lewis, 2004). Hershkovitz (pers. comm., February 2005) indicates that current research on suspected tuberculous skeletons in Israel is ongoing and involves ancient DNA, morphological and histological analysis.

c) Jordan

In Jordan, like Israel, very little evidence for skeletal TB has been identified. Ortner, in 1979, reported TB in the sphenoid bone of a 6-7 year old child and the spine of an 18 year old male from Early Bronze Age (3150-2200 BC) Bab edh-Dhra' (92 burials), the second oldest in the

world; current work is identifying further cases of possible TB in children but based on non-specific changes (Don Ortner, pers. comm., February 2005). El-Najjar et al. (1997) has also reported three TB-like cases from the Pre-Pottery Neolithic C levels at'Ain Ghazal, dated to 8100-7600 BP. Those affected were an adult male of 30 years old (5^{th} cervical vertebra), a 20-25 year old adult (5^{th}-7^{th} cervical vertebrae) and an old adult female (2^{nd} thoracic). Although reported as TB, there could be many differential diagnoses for these individuals (Hershkovitz and Gopher, 1999). Clearly, more work needs to be undertaken on these potentially early examples, although recent investigations indicate that the specimens have been 'lost' (Jerry Rose, pers. comm., 2005).

Unfortunately, additional data such as age at death, sex, and cultural associations for skeletons with evidence of TB from the Eastern Mediterranean are incomplete. Therefore detail biocultural interpretations must await further information.

Conclusions

In the Eastern Mediterranean TB first appeared in Egypt at a time when animals had been domesticated and people were also utilising their secondary products. Thus, those whose occupations brought them into proximity with animals may have been at risk for TB. There is further evidence for skeletal TB in Israel and Jordan, but it is less frequent. Lactose intolerance and lack of consumption of meat and milk may be a factor in these low frequencies, but ancient DNA analysis may, in the future, provide us with more accurate data. It is simply not possible to discuss age and sex and TB patterning, but we have noted high status people in Thebes (Egypt) having TB, thus showing how TB could cut across social barriers (Zink et al., 2003). Whether mobility affected TB occurrence is impossible to say, but stable isotope analysis may help address this issue in the future. Clearly, with respect to TB, there is still much research to do in the Eastern Mediterranean; this is mainly concerned with identifying true frequency rates, identifying TB in non-human remains and, most importantly, correlating cultural contextual data with the biological evidence.

TB, a disease that the West had thought it had all but conquered only about 20 years ago, shows little inclination to decline during the first years of the 21^{st} century. We have learned much about TB's history, but the most important factors in the Eastern Mediterranean past enabling TB to flourish were probably population density, sedentism, and contact with animals.

We have several general recommendations for future studies of skeletal TB in antiquity. Case reports should provide sufficient detail for independent evaluation. Rib lesions, while not pathognomonic, appear to show a strong correlation with pulmonary TB in clinically-documented collections. To date, few studies of pathology from the Eastern Mediterranean have considered rib pathology. Everybody working in palaeopathology needs to standardise data collection protocols (Buikstra and Ubelaker, 1994), be careful of their recording methods and their diagnoses (Ortner, 1991), and provide data in such a way that real prevalence rates for TB can be formulated (how many spines observed were affected?). Taking a population based, and more problem oriented perspective on TB would also move people away from considering "interesting" cases of TB scattered around the globe (Larsen, 1997). A more nuanced approach to considerations of biocultural contexts is also to be recommended.

Biomolecular methods of diagnosis in palaeopathology have clearly advanced the discipline in interesting ways. Most work to date on TB has concentrated on the actual diagnosis of TB (Salo et al., 1994; Baron et al., 1996; Taylor et al., 1996; Nerlich et al., 1997; Braun et al., 1998; Faerman et al., 1997; Gernaey et al., 1999), differentiation of bovine and human TB (Taylor et al., 1997), and very recently trying to link bone changes to an early stage in TB development in skeletons (Haas et al., 2000). Particularly exciting is the ability to diagnose TB in human remains where there are no skeletal lesions and to identify different mycobacterial species. The most convincing of these biomolecular studies involves verification in separate laboratories, detailed publication of protocols, and rigorous peer reviews of both methodologies and results.

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